Step 4 of 4: Abstract Preview

Print / Close window

Abstract Preview

ESC CONGRESS 2020

Doctor Carlos Bueno Beti (EUD ID : 1023070)
Institute Of Molecular And Clinical Sciences
St Georges University of London
SW17 ORE - Greater London United Kingdom of Great Britain & Northern Ireland
Phone : +44 004407851993915 -
Email : cbuenobe@sgul.ac.uk

Title : Cardiovascular phenotyping of the first mouse model of Sarcoidosis

Topic : 17.1 - Myocardial Disease – Pathophysiology and Mechanisms

Category : Bench

Option : Young Investigator Award (YIA) Basic Science

Funding Acknowledgements : - Type of funding sources: Foundation - British Heart Foundation - PG/18/27/33616 - I agree that this information can be used as submitted and made available online within the context of ESC research projects

C. Bueno Beti[1], C. Lim[2], A. Protonotarios[3], A. Kiss[4], MN. Sheppard[1], P L. Szabo[4], E. Behr[1], O. Hamza[4], B. Podesser[4], T. Weichhart[2], A. Asimaki[1] - (1) St George's University of London, Clinical Cardiology Academic Group, Molecular and Clinical Research Science Institute, London, United Kingdom of Great Britain & Northern Ireland (2) Medical University of Vienna, Center for Pathobiochemistry and Genetics, Vienna, Austria (3) University College London, Institute of Cardiovascular Science, Clinical Science Research Group, London, United Kingdom of Great Britain & Northern Ireland (4) Medical University of Vienna, Center for Biomedical Research , Vienna, Austria

Introduction: Sarcoidosis is a potentially life-threatening, inflammatory, granulomatous disease that affects multiple organs including the heart. Heretofore, its unknown etiology had hindered the creation of experimental models and the understanding of the molecular mechanisms of pathogenesis behind it.

Purpose: to extensively phenotype the heart of the first mouse model of sarcoidosis created through deletion of the tuberous sclerosis 2 (Tsc2) gene in the CD11c-positive macrophage population.

Methods: Tsc2flflCD11c-Cre+ (Tsc2KO; n=7) and Tsc2flflCD11c-Cre- (Tsc2WT; n=7) mice were subjected to echocardiography at 25 weeks of age (woa) to assess myocardial dimensions and function. Hearts of 13 and 25woa animals were subjected to histological and immunological stains to assess tissue changes, subtype inflammatory infiltrates and examine the localization of key proteins shown to be re-distributed in patients.

Results: At 13 woa, TSCKO animals show inflammatory infiltrates; subtyped mainly as macrophages as well as evidence of myocyte destruction. At 25 woa, the number of inflammatory cells is significantly higher and there is heavy fibrotic replacement primarily in the septum and trabeculae. Older animals also show giant cells and non-necrotizing granulomas. The hearts show heterogeneous gap junction remodeling known to constitute an arrhythmogenic substrate and lack of immunoreactive signal for the desmosomal protein plakoglobin from the cell-cell junctions just as described in patients. The left ventricular ejection fraction and LV morphology was not significantly different between the two groups (EF: 64±4% in Tsc2KO vs 64±2% in Tsc2WT; LV end-systolic diameter: 4.51±0.54mm in Tsc2KO vs 4.59± 0.29mm in Tsc2WT). However, there was a strong trend towards increasing filling pressure (E/e´ratio; 14.24±4.01 vs 12.15±2.54) and mean pulmonary pressure (21± 6 vs 18±3 mmHg) in TSCKO mice compared to controls suggesting diastolic dysfunction.

Conclusion: Hearts of the Tsc2flflCD11c-Cre+ animals show a phenotype highly reminiscent of cardiac sarcoidosis

» Rules and Regulations

☐ I hereby certify that this abstract has not been previously published or presented at any international congress and that I have read and approved the Abstract Submission Rules of the Abstract Submission Service and the Web Site Terms Conditions.